Glaucoma Research Society *of* Canada

We Support New Ideas

2009 RESEARCH GRANTS

THANKS TO OUR DONORS RESEARCHERS RECEIVE MORE THAN $205,000

Dr. Graham Trope, founder of the Glaucoma Research Society and chair of its Scientific Advisory Committee, recently announced the Society's 2009/2010 research grants for the following projects:

- Determining the Usefulness of the Heidelberg Retina Tomograph (HRT) in Monitoring Glaucoma Progression
- Mapping the Lymphatic Outflow Pathway in the Mouse Eye
- Studying the Awareness and Knowledge of Glaucoma among Black People in Toronto
- Studying the Association between Prescription Drugs containing Sulpha and Glaucoma
- Studying the Role of Immune Cells in Retinal Cell Survival
- Studying the Role of the Protein, Endothelin-1, (ET-1) in Glaucoma
- Inhaling Carbon Dioxide and Its Effect on Blood Vessels in the Eye
- Studying Nerve Growth Factors and Receptors in Glaucoma
- Determining if Regulating Endocannabinoid Levels Provides Retinal Protection following Ischemia and Optic Nerve Injury
- Evaluating Long-Term Corneal Cell Loss associated with Glaucoma Surgeries
- Studying the Response of Human Optic Nerve Cells to Different Modes of Mechanical Strain
- Comparing Different Types of Tonometry following Corneal Surgery

Determining the Usefulness of the Heidelberg Retina Tomograph (HRT) in Monitoring Glaucoma Progression

The HRT produces a three-dimensional map of the optic nerve and retina, and can be used to detect changes in the optic nerve and retina over time.Previous studies have shown it to be useful for detecting changes due to glaucoma. However, when compared to other techniques to evaluate the optic nerve such as stereophotography, the HRT was found to only somewhat agree.

Our study compares HRT to stereophotography to determine how good each one is at seeing and documenting changes in the optic nerve over time due to glaucoma.

A total of 75 patients have been recruited. Initially, 41 of these patients were showing changes in the optic nerve, only on the HRT, while their stereophotographs were stable. The optic nerves of 34 patients were stable on both the HRT and the stereophotographs.

During the study follow-up period of about two years, stereophotography documented changes in the optic nerves in only four of the 75 patients. Because glaucoma is generally a slowly progressing disease, our patients will be followed up at six to nine month intervals for an additional two years.

Using HRT to start early medication or to change management of the disease requires knowing how well HRT predicts the development of visual loss. The results of this study may affect the management of glaucoma patients by optimizing the follow-up of people with this disease and by starting appropriate and more individualized treatments. Early treatment is crucial for preventing further visual loss in patients with glaucoma or high pressure inside the eye.

– Dr. Dimitrios Kourkoutas; Dr. Yvonne M. Buys, University of Toronto, ON

Mapping the Lymphatic Outflow Pathway in the Mouse Eye

Current approaches to treating glaucoma are designed to lower pressure in the eye, either by reducing fluid formation and/or improving fluid drainage out of the eye. The body's lymphatic circulation carries fluids out of tissues, and is said to be absent in hair, nails and the eye. Challenging the belief that a lymphatic system does not exist inside the eye, we have discovered lymphatics in an area at the front of the human eye where fluid is known to exit.

Using various tracers, we will study lymphatics in the mouse eye to understand how and where these channels move fluid out of the eye. We predict that lymphatics can be manipulated to lower eye pressure. This would represent a major breakthrough for new glaucoma treatments to prevent vision loss.

– Dr. Neeru Gupta, Dr. Yeni H. Yücel, St. Michael's Hospital, Toronto, ON

Studying the Awareness and Knowledge of Glaucoma among Black People in Toronto

Black people are an established high risk group for glaucoma. This study aims to find socio-demographic factors associated with lack of awareness of glaucoma and lack of knowledge of three glaucoma risk factors (people aged 40 years and over; people of African origin; people with a family history of glaucoma) among Black people in Toronto.

To conduct this study, we will distribute a self-administered questionnaire about glaucoma to 800 Black participants, 35 years or older.

We believe that an informed public is more likely to seek early medical assistance before experiencing irreversible vision loss. This study will be the first in the world to identify needs and select areas for developing public education about glaucoma among Black people.

– Dr. Yaping Jin, University of Toronto, Toronto, ON

Studying the Association between Prescription Drugs containing Sulpha and Glaucoma

Drug induced ocular disorders are becoming an important public health issue. But information on ocular adverse events due to prescription drugs is limited despite the increase in the number of drugs used by older adults. One popular class of prescription drugs that may be associated with an increase in the risk of glaucoma are sulpha-based drugs including various anti-hypertensives, antibiotics and anti-epileptic drugs.

Using the British Columbia Linked Health Databases as the main data source, we will study the risk of glaucoma with three drugs: thiazide diuretics; sulfamethaxazole; and topiramate. This will be the first population-based study quantifying the risk of glaucoma with these drugs.

– Dr. Mahyar Etminan, University of British Columbia, Vancouver, BC

Studying the Role of Immune Cells in Retinal Cell Survival

Immune cells in the retina protect retinal cells from infection and disease. In animal models of glaucoma, immune cells become active when retinal cells are lost. It is widely believed that the immune cells secrete toxic substances that worsen the disease.

Our recent research shows that immune cell activation is an early event in the animal model of glaucoma, and that retinal cell death continues even after the immune cells return to their resting state. We hypothesize that immune cells may become activated in an effort to increase retinal cell survival by removing cellular debris and by secreting survival factors.

Our research will determine if immune cell activation is beneficial, or detrimental, to retinal cell survival in glaucoma. We will use drugs to inhibit or activate immune cells in animal models of glaucoma and measure retinal cell death. Our studies will lead to new glaucoma therapies aimed at controlling the activation of immune cells.

– Dr. Alexander K. Ball, McMaster University, Hamilton ON

Studying the Role of the Protein, Endothelin-1 (ET-1) , in Glaucoma

Increased levels of ET-1 have been found in the eyes and blood of patients with glaucoma. Studies in animals suggest that ET-1 can interfere with the normal function of the optic nerve and lead to the death of nerve cells in the eye. How ET-1 affects the optic nerve is not clear. Recent studies suggest ET-1 may act on astrocytes, cells that maintain the environment in which nerve cells live.

Our study will determine if ET-1 can influence the level of calcium ions in astrocytes in an intact optic nerve. The optic nerve is a thick, 3-D structure. To visualize astrocytes deep within the nerve, we will use dyes, which become brighter when the levels of calcium ions increase, and time -lapse laser-scanning confocal microscopy.

Evidence that ET-1 increases calcium ions within optic nerve astrocytes would add to the growing evidence that astrocytes are a target of elevated ET-1 during glaucoma and, therefore, a potential focus for therapeutic intervention.
– Dr. Xu Wang, Dalhousie University, Halifax, N.S.

Inhaling Carbon Dioxide and its Effect on Blood Vessels in the Eye

Some glaucoma patients have unstable or inadequate blood supply to the nerves at the back of the eye. Non-invasive, laser-based optical instruments are used with various stimuli to assess blood flow in the eye. One stimuli involves inhaling safe amounts of carbon dioxide. Carbon dioxide normally results in widening the blood vessels, increasing blood flow to the eye.

Our study will determine the effect of inhaling carbon dioxide on blood vessels of patients with glaucoma and of age-matched subjects without glaucoma. Preliminary results suggest that the response of the retinal blood vessels in the two groups is distinctly different.
– Dr. Chris Hudson, Dr. John G. Flanagan,University of Waterloo, Waterloo, ON

Studying Nerve Growth Factors and Receptors in Glaucoma

We have discovered that cells in a major vision centre of the brain (lateral geniculate nucleus – LGN) may die in glaucoma. The LGN, an important source of nerve growth factors, supports the health of nerve cells inside the eye. LGN degeneration may contribute to glaucoma worsening due to decreased levels of these factors.

We will study different nerve growth factors and receptors in the LGN to detect those most affected in glaucoma. This information may lead to new nerve growth factor treatment strategies to prevent vision loss in glaucoma
– Dr. Yeni H. Yücel, Dr. Neeru Gupta, St. Michael's Hospital, Toronto, ON

Determining if Regulating Endocannabinoid Levels Provides Retinal Protection after Ischemia and Optic Nerve Injury

Abnormal ocular blood flow may contribute to the development and progression of vision loss in glaucoma.

Local alterations in endocannabinoid levels are critical in regulating vascular tone and blood flow. Activating cannabinoid receptors in the eye decreases intraocular pressure and is associated with neuroprotection. Endocannabinoid metabolic enzyme inhibitors increase the levels of endocannabinoids in the eye by preventing the degradation of endocannabinoids at sites of production.

We are examining whether manipulating the endocannabinoid system using enzyme inhibitors can decrease vascular and neuronal damage in experimental models of retinal blood vessel occlusion and optic nerve injury. This research has relevance to the discovery of novel therapeutics for the treatment of glaucoma and retinal diseases involving vascular dysregulation.
– Dr. Melanie E.M. Kelly, Dalhousie University, Halifax, N.S.

Evaluating Long-Term Corneal Cell Loss associated with Glaucoma Surgeries

Preserving corneal endothelial cell function is a major goal of ocular surgery. Excessive endothelial cell loss and damage associated with intraocular surgery can lead to corneal edema, decreased corneal clarity and loss of visual acuity, often requiring corneal transplantation to restore normal vision.

Current treatment of glaucoma is directed toward decreasing intraocular pressure through the use of eye drops, laser treatment and surgery.

Trabeculectomy and glaucoma drainage devices are the most common glaucoma surgeries performed worldwide. The goal of these surgeries is to direct the aqueous flow from the anterior chamber into the subconjunctival space to control intraocular pressure.

Corneal endothelial cells obtain nourishment from the aqueous fluid. Both trabeculectomy and glaucoma drainage devices disrupt an otherwise well-maintained aqueous humour dynamic by redirecting the aqueous fluid. This can harm corneal endothelial cells after glaucoma surgery.

The goal of this study is to evaluate the long-term corneal endothelial cell loss associated with different glaucoma surgeries. This will be done using the gold standard technique of specular microscopy, as well as a newer technique of *in vivo* confocal microscopy.
– Dr. Lesya Shuba, Dalhousie University, Halifax, N.S.

Studying the Response of Human Optic Nerve Cells to Different Modes of Mechanical Strain

Mechanisms proposed to explain the development of optic nerve damage in glaucoma include the effects of mechanical stress at the level of the lamina cribrosa (LC) and insufficient vascular perfusion of the LC.

The specific aims of our research are focused towards developing models that will improve the understanding of how biomechanical factors affect the initiation and progression of glaucomatous optic neuropathy.
– Dr. John G. Flanagan, Toronto Western Research Institute, Toronto, ON

Comparing Different Types of Tonometry following Corneal Surgery

Goldman applanation tonometry (GAT) is affected by corneal thickness and rigidity, whereas the Pascal Dynamic Contour Tonometer (DCT) is reportedly able to accurately measure intraocular pressure (IOP) independently of corneal thickness and rigidity.

Patients who have undergone penetrating keratoplasty (PK) and Descemets stripping automated endothelial keratosplasty (DSAEK) procedures have markedly altered corneal thickness and rigidity. This makes IOP measurement with GAT difficult and inaccurate. In this study, we want determine if in these patients, IOP measurements with the Pascal DCT would be more accurate and clinically useful than GAT.

We will take IOP measurements pre-operatively on all patients undergoing PK and DSAEK procedures with both GAT and Pascal DCT to establish a baseline. At each post-operative visit, IOP will be measured with both techniques to determine if the Pascal DCT is more accurate.
– Dr. Ian Mcilraith, St. Joseph's Health Care Centre, London, ON